Occult infection in pseudarthrosis revision after spinal fusion

Burkhard, Marco D ; Loretz, Ruben ; Uçkay, Ilker ; Bauer, David E ; Betz, Michael ; Farshad, Mazda

Abstract: BACKGROUND CONTEXT Pseudarthrosis after attempted spinal fusion is yet not sufficiently understood and presents a surgical challenge. Occult infections are sometimes observed in patients with pseudarthrosis and no inflammatory signs of infection. The prevalence of such occult infection and its association with patient demographics and inflammatory markers are largely unknown. PURPOSE To determine the prevalence of unexpected low-grade infection in spinal pseudarthrosis revision surgery, and to evaluate whether such infection is associated with patient demographics and inflammatory markers. STUDY DESIGN Retrospective observational study. PATIENT SAMPLE One-hundred-and-twenty-eight patients who underwent thoracolumbar revision surgery due to presumed aseptic pseudarthrosis after spinal instrumentation. OUTCOME MEASURES Culture-positive infections or noninfectious pseudarthrosis. METHODS Samples were routinely taken for microbiological examination from all adults (n=152) who underwent revision surgery for presumed aseptic thoracolumbar pseudarthrosis between 2014 and 2019. A full intraoperative microbiological workup (at least three intraoperative tissue samples) was done for 128 (84%) patients, and these patients were included in further analyses. Patient characteristics, medical history, inflammatory markers, and perioperative data were compared between those with and without microbiologically-confirmed infection based on samples obtained during pseudarthrosis revision. RESULTS The microbiological workup confirmed infection in 13 of 128 cases (10.2%). The predominant pathogen was Cutibacterium acnes (46.2%), followed by coagulase-negative staphylococci (38.5%). The presence of infection was associated with the body mass index (30.9±4.7 kg/m^2 [infected] vs. 28.2±5.6 kg/m^2 [controls], p=.049), surgery in the thoracolumbar region (46% vs. 18%, p=.019), and a slightly higher serum C-reactive protein level on admission (9.4±8.0 mg/L vs. 5.7±7.1 mg/L, p=.031). Occult infection was not associated with age, sex, prior lumbar surgeries, number of fused lumbar levels, American Society of Anesthesiologist score, Charlson Comorbidity Index, presence of diabetes mellitus, and smoking status. CONCLUSIONS Occult infections were found in 10% of patients undergoing pseudarthrosis revision after spinal fusion, even without preoperative clinical suspicion. Occult infection was associated with higher body mass index, fusions including the thoracolumbar junction, and slightly higher C-reactive protein levels. Intraoperative microbiological samples should be routinely obtained to exclude or identify occult infection in all revision surgeries for symptomatic pseudarthrosis of the spine, as this information can be used to guide postoperative antibiotic treatment.

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Clinical Study

Occult infection in pseudarthrosis revision after spinal fusion

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Abstract

BACKGROUND CONTEXT: Pseudarthrosis after attempted spinal fusion is yet not sufficiently understood and presents a surgical challenge. Occult infections are sometimes observed in patients with pseudarthrosis and no inflammatory signs of infection. The prevalence of such occult infection and its association with patient demographics and inflammatory markers are largely unknown.

PURPOSE: To determine the prevalence of unexpected low-grade infection in spinal pseudarthrosis revision surgery, and to evaluate whether such infection is associated with patient demographics and inflammatory markers.

STUDY DESIGN: Retrospective observational study.

PATIENT SAMPLE: One-hundred-and-twenty-eight patients who underwent thoracolumbar revision surgery due to presumed aseptic pseudarthrosis after spinal instrumentation.

OUTCOME MEASURES: Culture-positive infections or noninfectious pseudarthrosis.

METHODS: Samples were routinely taken for microbiological examination from all adults (n=152) who underwent revision surgery for presumed aseptic thoracolumbar pseudarthrosis between 2014 and 2019. A full intraoperative microbiological workup (at least three intraoperative tissue samples) was done for 128 (84%) patients, and these patients were included in further analyses. Patient characteristics, medical history, inflammatory markers, and perioperative data were compared between those with and without microbiologically-confirmed infection based on samples obtained during pseudarthrosis revision.

RESULTS: The microbiological workup confirmed infection in 13 of 128 cases (10.2%). The predominant pathogen was *Cutibacterium acnes* (46.2%), followed by coagulase-negative staphylococci (38.5%). The presence of infection was associated with the body mass index (30.9 ± 4.7 kg/m^2 [infected] vs. 28.2 ± 5.6 kg/m^2 [controls], p=.049), surgery in the thoracolumbar region (46% vs. 18%, p=.019), and a slightly higher serum C-reactive protein level on admission (9.4 ± 8.0 mg/L vs. 5.7 ± 7.1 mg/L, p=.031). Occult infection was not associated with age, sex, prior lumbar surgeries, number of fused lumbar levels, American Society of Anesthesiologist score, Charlson Comorbidity Index, presence of diabetes mellitus, and smoking status.

CONCLUSIONS: Occult infections were found in 10% of patients undergoing pseudarthrosis revision after spinal fusion, even without preoperative clinical suspicion. Occult infection was associated with higher body mass index, fusions including the thoracolumbar junction, and slightly higher C-reactive protein levels. Intraoperative microbiological samples should be routinely obtained to exclude or identify occult infection in all revision surgeries for symptomatic

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pseudarthrosis of the spine, as this information can be used to guide postoperative antibiotic treatment.

Keywords: *Cutibacterium acnes* Occult infection; *Propionibactrium acnes* Pseudarthrosis; Revision surgery; Spine; Spondylodesis

Introduction

Spinal fusion represents one of the most frequently used technique to treat spinal degenerative diseases, deformity, trauma, infection, and tumor [1,2]. Revision surgery after spinal fusion is required in up to 45% of cases, depending on the length of follow-up [3−5]. One of the most important and challenging reasons for revision surgery is pseudarthrosis [3,6,7], namely failure of adequate bony fusion. Possible reasons for pseudarthrosis are insufficient primary stability of the implant construct, spinal dysbalance, long-construct fusion, insufficient bone quality, infection, smoking, and long-term steroid use [8−11]. However, the factor causing pseudarthrosis after attempted spinal fusion is often not identifiable.

Particularly low-grade infections can clinically be "occult" but present in 9% to 56% of spinal fusion revision cases [12−17]. The bacteria most frequently detected in low-grade orthopedic implant infections are *Cutibacterium acnes* and coagulase-negative staphylococci [12,18]. However, colonization by these bacteria in a minority of intraoperative tissue samples is also possible, and their mere presence *per se* is not proof of infection. Clinicians and microbiologists must assess the plausibility of a symptomatic low-grade infection and resultant need for long-term targeted antibiotic therapy versus the possibility of contamination and therefore unnecessary exposure to antibiotics [19].

In pseudarthrosis revision surgery, intraoperative samples are not taken unless infection is suspected. Therefore, the true prevalence of infections underlying pseudarthrosis is largely unknown. This knowledge gap results in diverse diagnostic protocols between institutions. Some surgeons argue that the prevalence of infection in pseudarthrosis is low if not clinically suspected, and therefore taking intraoperative samples will only produce potential false-positive suspicion and unneeded antibiotic treatments. In contrast, other surgeons believe that the rate of occult infections is higher than assumed, and so standardized microbiological workup is mandatory in pseudarthrosis revision. We aimed to evaluate the prevalence of occult infection in pseudarthrosis revision by performing a detailed microbiological workup in a retrospective series of spinal pseudarthrosis revision cases.

Material and methods

After receiving final approval from the local authorities (BASEC 2019-02077), we identified all adult patients who underwent revision surgery for symptomatic thoracolumbar pseudarthrosis between September 2014 and December 2019 in the institutional surgical spine register of a university spine center after initial thoracolumbar instrumentation via a posterior-only approach (n=152). Symptomatic pseudarthrosis was defined as failure of bony fusion or screw loosening on radiographs and computed tomography at >6 months after index fusion surgery and resultant mechanical back pain. The interval from the index operation until the revision for pseudarthrosis had to be at least 6 months to avoid inclusion bias of early infections. Asymptomatic patients, patients with incomplete clinical, intraoperative, or laboratory follow-up, and patients lacking intraoperative microbiological tissue sampling were excluded (n=24). Thus, 128 (84.2%) patients were included in the analyses. Demographic data such as age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and the Charlson Comorbidity Index (CCI) [20] were documented. In addition, the number of prior lumbar surgeries, number and localization of the previous fused levels, duration of the revision surgery, length of hospital stay, blood loss, and rehabilitation were recorded.

During pseudarthrosis revision surgery, at least three different tissue samples were taken for microbiological investigations. Two tissue samples were routinely gathered from the posterolateral pseudarthrosis area and one bony tissue sample from the lamina or pedicle of the same level. At the surgeon's discretion, additional samples were obtained from adjacent levels depending on the intraoperative impression and the patient's overall clinical presentation. Additionally, the removed hardware was sent for sonication [21,22]. The patients were not receiving therapeutic antibiotic therapy before revision surgery, as no infection was suspected (as per the inclusion criteria). Preoperative routine antibiotic prophylaxis (cefuroxime or in the case of penicillin-allergy: Vancomycin or clindamycin) was given in accordance with the routine protocol for all spinal procedures in our institution. Microbiological samples were incubated for 14 days for aerobic and anaerobic cultures. The routine bacterial culturing over 14 days is independent of the degree of suspicion for *C. acnes* or other pathogens at our institution. The microbiological results, number of positive specimens, and postsonication number of colonies were recorded. Histology or scintigraphy exams were adjunctive, and we did not distinguish between a culture result or a growth in enrichment broth only. The time to culture growth was not documented. In accordance with local microbiological custom, a pseudarthrosis was considered infected if the same bacterial species was identifiable in at least two intraoperatively obtained tissue samples and/or when at least 50 colonies of a bacterial species grew in the sonication fluid. The sonication was not only used to identify a possible causative pathogen, but also to define the presence of infection *per se*. Cases in which all tissue cultures remained negative but a sonication broth grew more than 50 colonies per mL were also defined as infected. The decisive cutoff of 50 colonies/mL originated from interinstitutional expert opinions and a landmark paper advocating that a threshold of 50 colonies/mL equaled a sensitivity of 68% and a specificity of 99% for an established prosthetic joint infection in removed arthroplasties [23]. In the present study, the clinical (intraoperative) assessment of the surgeon and/or the opinion of the infectious disease physician were ignored.

Statistical analyses

Statistical analyses were performed using SPSS (version 25; IBM, Armonk, NY) and Stata (version 13.1; StataCorp, College Station, TX). Means and standard deviations were calculated for continuous variables that were normally distributed; ordinal variables were represented by frequencies (%). Intergroup comparisons were done using the Mann-Whitney U-test for continuous variables, and the Fisher exact test or the Chi^2 test for categorical variables. Due to the low number of infections or failures after surgical revision, we did not perform multivariate regression analyses. The level of statistical significance was set at $p<.05$ (for two-tailed analyses).

Results

The mean age of the 128 included patients was 65.2± 14.8 years (range, 19−86 years) and 45% were female. The average interval from the index surgery to elective pseudarthrosis revision was 31±33 months (range, 6−112 months). The patients had undergone an average of 2.6 previous lumbar/thoracolumbar spine surgeries (range, 1−10 surgeries) before the final pseudarthrosis revision, with a mean of 3.4±2.7 levels of attempted fusion (range, 1−15 levels). None of the patients had any antibiotic therapy prior to surgery except of the routine preoperative antibiotic prophylaxis.

The microbiological findings are summarized in Table 1. Bacterial growth was present in intraoperatively obtained tissue samples in 25 cases (19.5%). Of these, 12 cases had only a single positive culture and were rated as contaminations; two of these 12 cases had *C. acnes*, and eight had S*taphylococcus* species. The remaining 13 cases (10.2%) were classified as low-grade infections using the abovementioned criteria. Microbiologically, they were most commonly caused by *C. acnes* (six cases; 46.2%) and coagulase-negative staphylococci (five cases; 38.5%), followed by *Enterococcus faecium* (two cases; 15.4%). Among these 13 infected pseudarthroses, the diagnosis of infection was based on sonication results only in four cases, while nine cases had positive enrichment broth culture results. Histology was available for two of these 13 low-grade infections and was interpreted by the pathologists as chronic infection. Clinically, all 13 cases demonstrated excruciating pain and prominent point tenderness over the pseudarthrosis segment. An infectious etiology was not suspected by the radiologist or clinician pre- or intraoperatively in any of these 13 patients.

Table 1.
Microbiological findings from samples obtained during pseudarthrosis revision

	Overall positive samples	Occult infections
No. of patients	25/128 (19.5%)	13/128 (10.2%)
Microorganisms		
Cutibacterium acnes	8 (6.3%)	6 (4.7%)
Enterococcus faecium	2 (1.6%)	2 (1.6%)
Coagulase-negative staphylococci	13 (10.2%)	5 (3.9%)
S. epidermidis	8 (6.3%)	4 (3.1%)
S. lugdunensis	1 (0.8%)	1 (0.8%)
S. hominis	2 (1.9%)	0
S. saccharolyticus	1 (0.8%)	0
S. caprae	1 (0.8%)	0
S. warneri/pasteuri	1 (0.8%)	0
Micrococcus luteus	1 (0.8%)	0
Ralstonia pickettii	1 (0.8%)	0

Positive microbiologic results were all discussed in an interdisciplinary approach with the infectiology unit, specialized on musculoskeletal infectiology. If by definition an occult infection was uncovered, immediate targeted antibiotic treatment was initiated and was continued for three months for all patients. All patients found with a *C. acnes* infection were treated with oral clindamycin for 3 months. The antibiotic treatment of patients with *Staphylococcus* and *E. faecium* infections differed, depending on the microbiologic profile, resistogram, and patient's tolerability. None of the patients with an occult infection had any major complication related to the surgery or antibiotic treatment, nor did any of these patients require any further revision surgery at a mean follow-up of 3.6±1.9 years.

The preoperative laboratory findings are summarized in Table 2. Patients with occult low-grade pseudarthrosis infection had slightly elevated serum CRP levels compared with those with noninfected pseudarthroses (9.4±8.0 vs. 5.7±7.1 mg/L, p=.031). Infectious pseudarthrosis was more common in patients with a CRP level of >5.0 mg/L than in those with a CRP level of ≤5.0 mg/L (63.6% vs. 33.0%, p=.049). Patients with occult infection had a slightly higher BMI than those with aseptic pseudarthrosis (30.9 vs. 28.2 kg/m^2, p=.049). Standard serum laboratory markers were not capable of identifying infectious pseudarthrosis. In particular, there was no significant difference between occult infected and noninfected pseudarthroses in the serum leukocyte and hemoglobin counts on admission.

Table 2.
Preoperative laboratory markers

Variable	Aseptic pseudarthrosis	Occult infection	p Value
No. of patients	115/128 (89.8%)	13/128 (10.2%)	
Leucocyte level >10.2 × 10^9/L	13.3%	30.8%	0.108
Mean leucocyte count (10^9/L)	7.5±2.2	8.3±2.1	0.16
C-reactive protein level >5.0 mg/L	33.0%	63.6%	**0.049**
Mean C-reactive protein level (mg/L)	5.7±7.1	9.4±8.0	**0.031**
Mean preoperative hemoglobin level (g/L)	135.8±14.0	136.9±14.6	0.836

Data are given as mean±standard deviation. Bold text indicates statistical significance.

Table 3.
Patient characteristics

Variable	Aseptic pseudarthrosis	Occult infection	p Value
No. of patients	115/128 (89.8%)	13/128 (10.2%)	
Age (years)	65.2±15.2	64.8±11.6	0.475
Female sex (%)	45.2	46.2	0.949
Mean body mass index (kg/m^2)	28.2±5.6	30.9±4.7	**0.049**
Current smoker (%)	4/89 (4.5%)	0/13 (0%)	1.0
American Society of Anesthesiologists score	2.7±0.6	2.7±0.5	0.753
Charlson comorbidity index	3.4±2.3	3.3±2.4	0.790
Diabetes (%)	15.7	15.4	1.0
Time since previous surgery (mo)	31.6±34.5	25.0±17.8	0.51
No. of prior surgeries	2.6±1.6	3.0±1.7	0.299
No. of prior levels fused	3.3±2.5	4.8±3.9	0.179
Thoracolumbar fusion (%)	18.3	46.2	**0.019**
Sacral fusion (%)	61.7	61.5	1.0

Data are given as mean±standard deviation, unless otherwise indicated. Bold text indicates statistical significance. Current smoker means behavioral smoking at the time of revision surgery.

The patient characteristics are summarized in Table 3. Infection was significantly more common in patients with spinal fusion involving the thoracolumbar junction (56% vs. 18.3%, p=.019), but there was no significant difference between cases of infected and noninfected pseudarthroses regarding the incidence of lumbosacral level fusion (61.7% vs. 61.5%, *p*=1.0). There were no significant differences between patients with occult infection versus those with aseptic pseudarthroses regarding mean age (65.2±15.2 vs. 64.8±11.6 years), mean ASA score, proportion of females (45.2% vs. 46.2%), presence of diabetes, and smoking status. As shown in Table 4, the two groups also had a similar time delay between index surgery and pseudarthrosis revision surgery (31.6±34.5 months vs. 25.0±17.8 months, p=.510), number of previous spine surgeries (2.6±1.6 vs 3.0±1.7, p=.299), and number of levels fused (3.3±2.5 vs. 4.8±3.9, p=.179).

Discussion

The present study aimed to evaluate the prevalence of occult infections in pseudarthrosis revision by performing detailed microbiological workup in a retrospective series of spinal pseudarthrosis revisions. Without having any clinical suspicion of infection preoperatively, we have found occult low-grade infections in 10% of adult patients with

Table 4.
Perioperative data

Variable	Aseptic pseudarthrosis	Occult infection	p Value
No. of patients	115/128 (89.8%)	13/128 (10.2%)	
Length of surgery (min)	193±71	188±89	0.705
Estimated blood loss (mL)	475±340	354±239	0.262
Prepostoperative difference in hemoglobin level (g/L)	32.0±19.4	28.2±12.3	0.344
Length of hospitalization (d)	7.1±2.6	9.4±4.7	0.099
Referral to rehabilitation (%)	38.3	53.8	0.277

Data are given as mean±standard deviation, unless otherwise indicated.

symptomatic pseudarthrosis following attempted spinal fusion. These infections would have been missed and remained insufficiently treated if routine microbiological sampling had not been performed in all pseudarthrosis revisions. We implement the findings of this study into our clinical practice by (1) routinely obtaining at least three deep tissue samples and sending the removed hardware to sonication, (2) discussing the microbiological results of each patient in an interdisciplinary approach with the infectiology unit and immediately initiate a targeted antibiotic treatment if needed, and (3) being aware of a potential infectious etiology of spinal pseudarthrosis, especially in patients with the associated risk factors outlined in this study.

Occult low-grade infection in spinal revision surgery has been reported [6,7−11,17,18]. Hu et al. [7] found positive cultures indicating subclinical infection in 15 of 162 revision spine surgery cases (9.3%). Shifflet et al. and Steinhaus et al. [13−15] evaluated 595 cases of spinal revision for various indications. Tissue samples were obtained in 112 cases (18.8%), and were positive in 45 of these cases (40.2%). Of the 112 cases in which tissue samples were obtained, pseudarthrosis was the most common reason for revision surgery (49.1%), and the cultures were positive in 55.6% of pseudarthrosis cases. The authors concluded that patients with pseudarthrosis are at higher risk of subclinical infection [13, 15]. However, as cultures were only obtained in 18.8% of their cohort, their results may be biased by unknown confounding factors, and the pathogenicity of the microbiological results remains unclear. Ohrt-Nissen et al. [17] yielded positive microbiological cultures in 52% of spinal pseudarthrosis cases, but did not confirm that pseudarthrosis was significantly associated with occult infection in comparison with other indications for spinal revision surgery. Pumberger et al. [16] reported positive sonication cultures in 45.2% of presumed aseptic revision spine surgeries. The causal relationship between the microbiological findings with the symptoms for each of these episodes remains unknown. In summary, previous studies have included relatively inhomogeneous cohorts with various indications for revision surgery. Although pseudarthrosis has been identified as being more commonly associated with underlying low-virulent bacteria, occult infections in pseudarthrosis revision surgery has not been investigated *per se* [15]. Thus, the present findings add to the knowledge needed to decide whether routine microbiological sampling should be performed in spinal pseudarthrosis revision.

The pathogens identified in the present study are usually considered to have low virulence. The presumed mechanism of infection is material-related surgical site infection [6], as the main pathogens were mostly cutaneous in origin. The most common pathogen was *C. acnes* (46.2%), followed by coagulase-negative staphylococci (38.5%), both of which have a cutaneous origin. *C. acnes* is a slow-growing, microaerophilic Gram-positive rod that is frequently considered to be a contaminant [19, 24−27]. However, several studies have implicated *C. acnes* as a cause of vertebral osteomyelitis, spondylodiscitis, and low-grade infection after spinal surgery [7,28,29].

Because no infectious etiology was suspected in the investigated cohort, none of our patients had a preoperative systemic antibiotic therapy. They only witnessed the first dose of the routine preoperative antibiotic prophylaxis, which is cefuroxime 1.5 g parenterally except in the case of penicillin-allergy, in which either vancomycin or clindamycin were given. This single dose of a narrow-spectrum cephalosporine, administered approximatively 20−40 minutes before sampling, might theoretically alter the microbiological results. Withholding antibiotic prophylaxis until tissue samples are obtained to optimize culture results remains a matter of debate. The expert's world is divided between those in favor of a preoperative prophylaxis and those who remain against. Today, the exact scientific answer is missing. Al-Mayahi et al. [30] compared the epidemiology of intraoperative microbiological results between orthopedic infections with and without prior antibiotic use. Among 2740 cases, preoperative antibiotic exposure (43% of patients) was associated with significantly more culture-negative results (odds ratio 2.8), more nonfermenting rods and skin commensals. They have further found that even a single preoperative dose of antibiotic was significantly associated with subsequent culture-negative results compared with episodes without preceding prophylaxis. However, patient characteristics and health complaint did differ between the two cohorts (with and without preoperative antibiotic treatment) which may limit this finding. In contrast, several other studies with various study designs have shown, that preoperative antibiotic prophylaxis do not compromise the culture results in patients with septic as well as occult prosthetic joint infections [31−34]. According to Anagostopoulos et al. [35] the perioperative antibiotic prophylaxis does not compromise the microbiological yield of *C. acnes* in bone and joint infections, which was the most common pathogen in the cohort of the presented study. If the findings of these studies translate to the lumbar spine is uncertain. It is however proven, that preoperative antibiotic prophylaxis can efficiently avoid surgical site infections after spine surgery, as shown by multiple studies [36−38]. After weighing up the pros and cons, we thus continue to administer the routine preoperative prophylaxis before microbiological sampling in patients with low clinical suspicion of an infection such as in the investigated cohort of this study.

In the present cohort, a slightly higher BMI and slightly elevated CRP serum level on admission were somewhat correlated with the intraoperative identification of occult low-grade infection. Chronic, low-grade infections are not usually correlated with a high CRP level [12, 16]. Nevertheless, a recent study found significantly higher CRP levels in infected spinal revisions compared with aseptic revision surgeries [39]. However, the serum CRP level only had a low sensitivity (64%) and specificity (68%) regarding the prediction of spinal implant infection, even after applying optimized cutoff values [39]. We therefore believe that a slightly elevated CRP may be indicative at best, but does not prove that pseudarthrosis is caused by an underlying infection. Furthermore, the slightly elevated CRP level was still within normal ranges in most of the present cases. A slightly higher BMI has previously been identified as a risk factor for surgical site infection [40,41]. However, other described risk factors for postoperative surgical site infections such as older age, diabetes, malnutrition, ASA score, comorbidities and prior spine surgeries did not apply to the occurrence of an occult infection in our cohort [40−42]. Although, a trend toward higher number of prior fusion levels and prior spine surgical procedures was found in the occult infection group, this observation did not reach statistical significance, which is arguably due to the limited sample size. Male sex has also previously been identified as a risk factor for occult infection in spinal revision surgery [15], but this was not confirmed in our cohort. Such discrepancies between studies are most likely due to the highly select cohort included in the present study (only patients undergoing revision for pseudarthrosis) and the small sample size.

The present findings cannot be used to claim a causative link between the prerevision symptoms and the microbiological findings. The mere detection of *C. acnes* in deep intraoperative layers is not proof of infection. For example, up to 40% of all intraoperative samples from patients with uninfected shoulders harbor various quantities *of C. acne*s, of which the vast majority do not result in clinical infection, even without antibiotic treatment [19]. Therefore, the positive findings in 10% of our cases could be interpreted as contamination, while the symptoms were related to noninfectious aspects of pseudarthrosis. It is impossible to definitively distinguish between colonization and low-grade infection based on microbiological findings alone. We attempted to overcome this limitation by defining an occult infection as the identification of at least two positive cultures of the same pathogen in samples or a growth of 50 or more colonies in the sonication obtained intraoperatively. Besides harvesting tissue from each side of the posterolateral pseudarthrosis mass and one from the posterior arch, sampling was not further standardized. Thus, two positive samples do not entirely rule out a contamination, but represent a true infection by our definitions, which are in concordance to previous studies [13,21].

Some surgeons would argue that occult infections are self-limiting after implant removal or replacement and antibiotic treatment is redundant. As a matter of fact, the number needed to treat nor the number needed to sample to safe a patient from a detrimental postsurgical course due to an insufficiently treated or missed occult infection remains unknown. Also, no precise statement on cost-effectiveness of routine sampling, hardware sonication and subsequent antibiotic treatment can be made based on the current evidence. However, from our standpoint, the expenditures of routinely sampling and appropriate antibiotic treatment do not stand in any proportion to the estimated direct and indirect costs of possibly avoidable further complications in a patient cohort that has already had an undesirable medical course after a failed primary spinal fusion procedure. In our opinion, it should thus be regarded as a physician's duty of care to routinely obtain deep tissue samples in all pseudarthrosis revision cases even if it were less than one out of ten patients, that could get an accurate postoperative treatment regimen.

Keeping the abovementioned limitations in mind, the present study suggests that occult infections are present in 10% of revisions for pseudarthrosis after spinal fusion, even without any preoperative suspicion. The other factors somewhat associated with occult infection in this cohort were a slightly higher BMI, instrumentation including the thoracolumbar junction, and slightly higher CRP level (but still within the normal range). Based on these findings, we advocate the sampling of multiple deep tissue specimens for microbiological investigation in all spinal pseudarthrosis revisions, as targeted antibiotic treatment can subsequently be initiated in cases with otherwise occult infection.

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